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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/020,139	12/18/2001	Roxanne Duan	PF348C1	7037

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EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 03/24/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/020,139	DUAN ET AL.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,18-34 and 36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14,18-34 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 January 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 1/21/03 (Paper No. 9), is acknowledged.

Claims 1-14, 18-34 and 36 are pending.

Claims 1-14, 18-34 and 36 are under consideration in the instant application.

2. Applicant's submission of post filing date reference of Ashkenazi et al, (WO 00/53755 exhibit A) teaching that hPSP polypeptide was upregulated in primary colon tumors and in primary lung tumor has obviated the previous 35 U.S.C. 101 rejection of record in Paper No. 8, mailed on 10/22/02.

3. Applicant's submission of Rosen et al .(Patent application 09/912,292 on the IDS , paper No: 11) is acknowledged, however this citation has been crossed out as not appropriate for an IDS.

4. In view of the amendment, filed 1/21/03 (Paper No. 9) and statement by the attorney of record regarding permanence and availability of deposit cDNA clone, filed 1/21/03 (Paper NO:12), only the following rejections remain:

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-14, 18-34 and 36 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention essentially for the same reasons set forth in the previous Office Action, Paper No:8, mailed 10/22/02.

Applicant's arguments, filed 1/21/03 (Paper No. 9) have been fully considered, but have not been found convincing

Applicant asserts that : (i) it is not necessary for the claimed polynucleotide or any polypeptide encoded thereby, to be biological active or to be defined by functional properties in order to be fully enabled. Rather, the claimed polynucleotides needs merely have application in a single use; (ii) the skilled molecular biologist, enlightened by the teaching of the present specification, is more than capable of routinely determining whether a polynucleotide has uses.

Contrary to Applicant assertion, the issue raised in the previous Office Action was if one skilled in the art clearly would know how to make and use the invention. It is noted that the Specification as filed does not teach or suggest the use of the claimed polynucleotide in detecting the hPSP polypeptide in primary colon tumors and in primary lung tumor.

The specification discloses only specific nucleic acid molecules comprising a polynucleotide encoding at least a portion of the human Parotid Secretory Protein (hPSP) having the complete amino acid sequence of SEQ ID: 2 or the complete amino acid sequence encoded by the cDNA clone deposited in bacterial host as ATCC Deposit NO 97811 and nucleotide sequence (SEQ ID NO:1) determined by sequencing the deposited hPSP clone (pages 5-6 of the specification as filed).

The specification fails to provide guidance as how to make and use (1) *Any* isolated nucleic acid molecule, comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group recited in claim 1, or complete nucleotide sequence of SEQ ID NO:1 (claim 2), or nucleotide sequence in SEQ ID NO:1 encoding the hPSP polypeptide having the amino acid sequence in position –17 to +231 of SEQ ID NO:2 (claim 3), or nucleotide sequence in SEQ ID NO:1 encoding the mature form of the hPSP polypeptide having the amino acid sequence from about amino acid residue 1 to about amino acid residue 231 of SEQ ID NO:2 (claim 4); or complete nucleotide sequence of the cDNA clone contained in ATCC Deposit No 97811(claim 6), or nucleotide sequence encoding the hPSP polypeptide having the complete amino acid sequence except the N-terminal amino acid encoded by the cDNA clone contained in ATCC Deposit No 97811 (claim 7) or nucleotide sequence encoding the mature form of the hPSP (claim 8); (2) *any* isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95 % identical to a sequence selected from the group recited in claim 5; (3) an isolated nucleic acid molecule comprising a nucleic acid sequence which encodes an epitope-bearing portion of an hPSP polypeptide selected from the group recited in claim 9; (4) a method of making *any* recombinant vector , (claims 10 and 31), *any* recombinant vector (claims

11 and 31), a method of making *any* recombinant host cell (claim 12) and a recombinant host cell (claims 13 and 33) and a method for producing a hPSP (claims 14 and 34); (5) *any* isolated nucleic acid molecule comprising a polynucleotide having a sequence at least 95 % identical to a sequence selected from the group recited in claim 18; (6) *any* isolated polynucleotide comprising a nucleic acid sequence selected from the group recited in Claim 19, or comprising SEQ ID NO:1 (claim 22) or encoding a mature polypeptide (claim 24) or identical to the human cDNA contained in ATCC Deposit No. 97811 (claim 25) or encoding at least 50 contiguous amino acids of SEQ ID NO:2 (claim 27) or complementary to the polynucleotide of claim 19 (claim 28) ; (8) *any* isolated polynucleotide of claim 19, further comprising a hetorologus polynucleotide (claim 29), wherein said heterologous polynucleotide encodes a heterologous polypeptide (claim 30); (9) a composition comprising *any* isolated polynucleotide of claim 19 (claim 36) without undue experimentation.

There does not appear to be sufficient guidance in the specification as filed as to how the skilled artisan would make and use the various nucleic acids recited in the instant claims. A person of skill in the art would not know which sequences are essential and which sequences are non-essential. There is insufficient guidance to direct a person of skill in the art to select particular sequences or sequence lengths as essential for the function of nucleic acid sequence of SEQ ID NO:1 and polypeptide encoded by the amino acid sequence of SEQ ID NO: 2. Moreover, there is insufficient guidance as to which "isolated polynucleotide comprising a heterologous polynucleotide", recited in the claim 29 and which "heterologous polypeptide" recited in claim 30, would maintain the same function as polypeptide encoded by amino acid sequence of SEQ ID NO: 2.
Thus there appears to be insufficient guidance in the specification as filed to direct a person skill in the art to *select particular nucleotide sequence as encoding amino acids essential for the functional properties of the polypeptide. In addition, no functional properties of hPSP are even disclosed.*

Since the nucleic acid sequence of a polynucleotide determines its protein coding properties, predictability of which changes can be tolerated in a polynucleotide's nucleic acid sequence and still retain similar functions and properties requires a knowledge of, and guidance with regard to which nucleic acids within the full-length nucleotide sequence, if any, are tolerant of modification and which are conserved or less tolerant to modification, and detailed knowledge of the ways in which the product's structure relates to its functional usefulness. Because there is insufficient guidance in the specification as to which amino acids sequence within the full-length amino acid sequence of SEQ ID NO: 2, which encoded hPSP that after substitution, deletion or insertion will retain the same function, it is unpredictable to determine which polynucleotide comprising a polynucleotide sequence that encodes a polynucleotide sequence that has at least "95% identity" to the nucleic acid sequence, encoding the hPSP of SEQ ID NO: 2 will have similar function. Since the structure associated with functions of any polynucleotide mentioned above are not disclosed, predicting which polynucleotide that has at least 95% identity to the nucleic acid sequence , encoding the hPSP of SEQ ID NO: 2 having the same function as amino acid sequence of SEQ ID NO: 2 is well outside the realm of routine experimentation.

The instant Claims encompass fragments. For example, claim 18 recite a nucleic acid comprising of a fragment of at least 30 contiguous nucleotides from 48 to 793 nucleotides of nucleotide sequence of SEQ ID NO: 1 or a complement thereof ,claim 19 recite a nucleic acid sequence encoding a polypeptide of at least 30 contiguous amino acid of SEQ ID NO:2 and claim 27 recite a nucleic acid sequence encoding a polypeptide of at least 50 contiguous amino acids of SEQ ID NO:2. There is insufficient guidance as to which nucleic acid residue within the nucleic acid sequence mention above or amino acid sequence within a polypeptide encoded by amino acid sequence of SEQ ID NO: 2 are *essential for the functional properties of nucleic acid molecule or the encoded polypeptide.*

Skolnick et al. (Trends in Biotech., 18(1):34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2).

Ngo *et al* teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure will require guidance (see Ngo *et al.*, 1994, The protein Folding Problem and Tertiary Structure Prediction, pp.492-495). Similarly, Skolnick *et al.* (Trends in Biotech., 18(1):34-39, 2000) teach that sequence-based methods for function prediction are inadequate because of the multifunctional nature of proteins (see the abstract Page 34). Such a recitation does not require that the nucleic acid encode the full length sequence set forth in SEQ ID NO:1; but rather encompasses any nucleic acid sequence comprising either the full length of SEQ ID NO:1 or any contiguous nucleic acid residues. Without sufficient guidance, the changes which can be made in nucleic acid sequence of SEQ ID NO: 1 and still maintain activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

In re Fisher, 1666 USPQ 19 24 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

Reasonable correlation must exist between the scope of the claim and the scope of enablement set forth. Without sufficient guidance, the changes which can be made in the instantly recited nucleic acid sequences or proteins encoded by the recited nucleic acid sequences and still maintained the functional properties of SEQ ID NO: 1 and protein encoded by SEQ ID NO: 2 is unpredictable, as is the identity of which fragments would encode a functional polypeptide since the amino acids encoding a particular functional activity do not appear to have been identified;

thus the experimentation left to those skilled in the art is unnecessary, improperly, extensive and undue.

In view of the quantity of experimentation necessary, absence of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

7. Claims 1-14,18-20, 26-34 and 36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention essentially for the same reasons set forth in the previous Office Action, Paper No:8, mailed 10/22/02.

Applicant's arguments, filed 1/21/03 (Paper No. 9) have been fully considered, but have not been found convincing

Applicant asserts that : (i) The specification contains an adequate written description of the claimed polynucleotides since the instant specification defined the claimed genus through the recitation of the nucleic acid sequence of SEQ ID NO:1; (ii) Examiner has underestimate the level of skill in the art, since one skilled in the art can identify many species that the claims encompass.

Contrary to Applicants' assertions, the specification fails to provide sufficient guidance as to which core structure of SEQ ID NO: 1 is essential to maintain its functional activity and which changes can be made in the structure of SEQ ID NO: 1 and still maintained the same function. In addition: A) there is no indication of an isolated nucleic acid molecule variants with 95% identity to SEQ ID NO:1, and biologically active fragments, of SEQ ID NO: 1 on page 7, lines 1-23 page 18, line 1 to page 20, line 16 and at page 28 line 19 to page 29 line 2 that possesses that same functional properties as nucleic acid molecule of SEQ ID NO:1. Moreover, in contrast to applicants' assertions that the examiner position is nothing more than a misguided attempt to require Applicants to unduly limit the scope of their claimed invention; the examiner has relied upon adequate explanations with supporting evidence to maintain the rejection of record under 112, first paragraph, based upon the Forman factors. After evidence or arguments are submitted by the applicants in response, patentability is determined on the totality of the record, by a preponderance of the evidence with due consideration to persuasiveness of argument.

The Examiner notes that the claimed invention which is drawn to a genus of polynucleotide sequences may be adequately described if there is a (1) sufficient description of a representative number of species, or (2) by disclosure of relevant, identifying characteristics sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. To satisfy the disclosure of a "representative number of species" will depend on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of

the elements possessed by the members of the genus in view of the species disclosed. "Relevant, identifying characteristics" include structure or other physical and /or chemical properties, functional characteristics coupled with a known or disclosed correlation between function and structure, or a combination of such identifying characteristics sufficient to show the applicant was in possession of the claimed genus. (see Revised Guidelines for the Examination of Patent Applications Under the 35 U.S.C.112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No.4, pages 1099-1111, Friday January 5, 2001).

In the instant case, however, there is insufficient description or art-recognized correlation or relationship between the structure of the invention, the nuclei acid sequence of SEQ ID NO:1 that encodes polypeptide hPSP of SEQ ID NO:2 and it's function that is essential to the instant invention. Therefore, one of skill in the art would not envisage, based on the instant disclosure, the claimed genus of variants, wherein the variants are: (1) *Any* isolated nucleic acid molecule, comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group recited in claim 1, or complete nucleotide sequence of SEQ ID NO:1 (claim 2), or nucleotide sequence in SEQ ID NO:1 encoding the hPSP polypeptide having the amino acid sequence in position –17 to +231 of SEQ ID NO:2 (claim 3), or nucleotide sequence in SEQ ID NO:1 encoding the mature form of the hPSP polypeptide having the amino acid sequence from about amino acid residue 1 to about amino acid residue 231 of SEQ ID NO:2 (claim 4); or complete nucleotide sequence of the cDNA clone contained in ATCC Deposit No 97811(claim 6), or nucleotide sequence encoding the hPSP polypeptide having the complete amino acid sequence except the N-terminal amino acid encoded by the cDNA clone contained in ATCC Deposit No 97811 (claim 7) or nucleotide sequence encoding the mature form of the hPSP (claim 8); (2) *any* isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95 % identical to a sequence selected from the group recited in claim 5; (3) an isolated nucleic acid molecule comprising a nucleic acid sequence which encodes an epitope-bearing portion of an hPSP polypeptide selected from the group recited in claim 9; (4) a method of making *any* recombinant vector , (claims 10 and 31), *any* recombinant vector (claims 11 and 31), a method of making *any* recombinant host cell (claim 12) and a recombinant host cell (claims 13 and 33) and a method for producing a hPSP (claims 14 and 34); (5) *any* isolated nucleic acid molecule comprising a polynucleotide having a sequence at least 95 % identical to a sequence selected from the group recited in claim 18; (6) *any* isolated polynucleotide comprising a nucleic acid sequence selected from the group recited in Claim 19, or comprising SEQ ID NO:1 (claim 22) or encoding a mature polypeptide (claim 24) or identical to the human cDNA contained in ATCC Deposit No. 97811 (claim 25) or encoding at least 50 contiguous amino acids of SEQ ID NO:2 (claim 27) or complementary to the polynucleotide of claim 19 (claim 28) ; (8) *any* isolated polynucleotide of claim 19, further comprising a hetorologus polynucleotide (claim 29), wherein said heterologous polynucleotide encodes a heterologous polypeptide (claim 30); (9) a composition comprising *any* isolated polynucleotide of claim 19 (claim 36).

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 14 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention essentially for the same reasons set forth in the previous Office Action, Paper No:8, mailed 10/22/02.

Applicant's arguments, filed 1/21/03 (Paper No. 9) have been fully considered, but have not been found convincing.

Applicant asserts that the term "recombinant method" has a generally accepted meaning within the art.

Contrary to the applicant assertion, it is unclear how a method can be "recombinant" ? It is suggested that said phrase be change to " a method using recombinant techniques" for clarity and consistence with the disclosure of the specification.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is (703) 308-4232. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
March 20, 2003

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3/21/03